PATENT COOPERATION TREATY

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REC'D 10 NOV 2004
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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference BN 48 PCT	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/08359	International filing date *(day/month/year)* 29.07.2003	Priority date *(day/month/year)* 07.08.2002
International Patent Classification (IPC) or both national classification and IPC C12N15/86		
Applicant BAVARIAN NORDIC A/S et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
19.02.2004	09.11.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Valcarcel, R Telephone No. +49 89 2399-2368

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/08359

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-32 as originally filed

Claims, Numbers

1-28 as originally filed

Drawings, Sheets

1/7-7/7 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☒ contained in the international application in written form.

   ☒ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☒ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

   see separate sheet

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 13,14 (with respect to industrial applicability)

   because:

   ☒ the said international application, or the said claims Nos. 13,14 (with respect to industrial applicability) relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-17,27,28
	No:	Claims	18-26
Inventive step (IS)	Yes:	Claims	NONE
	No:	Claims	1-28
Industrial applicability (IA)	Yes:	Claims	1-12,15-28
	No:	Claims	NONE

2. Citations and explanations

see separate sheet

Re Item I

Amended claim 19 filed on 08-07-2004 with letter of 07-07-2004 goes beyond the disclosure in the international application as filed, contravening the requirements of Article 34 (2)(b) PCT. **Thus, amended claim 19 has not been considered for the establishment of the IPER.** Decision G0002/03 of the Enlarged Board of Appeal of the EPO establishes the requirements for allowability of disclaimers not having basis in the application as filed. An anticipation is considered as accidental if it is so unrelated to an remote from the claimed invention that the person skilled in the art would never have taken it into consideration when making the invention (see Headnote, section 2.1, second paragraph). **D1 and D2** do not satisfy this criteria of "accidental anticipation" since they **are not so unrelated** to the present application. The skilled person would have take them into consideration when making the invention. In fact D1 and D2 are used in the argumentation of lack of inventive step (see sections 3 to 3.3 of item V below). Section 2.3 of the Headnote of G0002/03 indicates that a disclaimer which is or becomes relevant for the assessment of inventive step adds subject-matter.

It is noted that in claim 1 there is also a disclaimer, but in this case, said disclaimer has basis in the application as filed.

Re Item III

Claims 13-14 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V

1. The document numbering corresponds to the order of citation in the search report.

2. The present application does not satisfy the criterion set forth in Article 33(2) PCT because **the subject-matter of claims 18-26 is not new** in respect of prior art as defined in the regulations (Rule 64 PCT).

2.1 Claim 18 refers to cells infected with an avipoxvirus and a vaccinia virus (it is noted that wild type vaccinia virus contain vaccinia host range genes). Since fowlpoxvirus (an avipoxvirus) can infect mammalian cells (see D3, page 443, right column, second paragraph), any cells naturally infected by a wild type vaccinia virus and a wild type avipoxvirus fall under the scope of these claims. Since both virus are abundant in

nature it is considered that said co-infection has happened many times. Thus, the subject-matter of claim 18 is not novel.

2.2 **D1** and **D2** disclose an avipoxvirus comprising a vaccinia host range gene (see e.g. abstract of D1). In particular, D1 and D2 disclose avipoxvirus which are disclaimed in claim 1 of the present application. D1 and D2 further disclose mammalian and avian cells infected with said vector (see e.g. figure 5 of D1). Thus D1 and D2 are prejudicial to the novelty of claims 19-26 of the present application.

3. The present application does not meet the requirements of Article 33(3) PCT since **the subject-matter of claims 1-28 does not involve an inventive step.**

D3 discloses the analysis of fowlpox (an avipoxvirus) host range restriction (see abstract). On page 444, left column, it is summarized that the overall "block" to productive fowlpox replication in mammalian cells appears to involve an inefficient gene expression.

Even further, on the last paragraph of page 444, D3 invites the skilled person to explore which mechanism explain the differences in efficacy as recombinant vectors between different avipoxvirus (in particular differences between fowlpoxvirus and canarypoxvirus are disclosed).

D4 discloses vaccinia host range genes (see abstract). Said genes confer the ability of vaccinia virus to replicate in particular cell types. Deletion of both C7L or KL1 from the wild-type vaccinia genome results in virus deficient for replication on human cells. Furthermore, it was well known in the art that deletions in host range genes, as vaccinia E3L, were associated to failures in replication (see abstract of **D6**; or **D5**, page 335, left column, first paragraph).

3.1 It is considered that the skilled person would have been motivated to combine the teachings of D3 and D4, and to include vaccinia host range genes (either E3L, disclaimed in claim 1 of the present application, or others) in avipoxvirus, in order to try to study the effect of such genes in avipoxvirus gene expression.

3.2 Furthermore, **D1 and D2** disclose that the expression of the vaccinia genes E3L and K3L resulted in an strong increase of antigen production (see abstract of D1). Said increment in expression is disclosed to be related to effects in transcription and

translation, in particular E3L appears important for mRNA stability (see e.g. from line 36 of page 11 to line 20 of page 12 of D2).

It is considered that the skilled person would have been motivated to include vaccinia host range genes in avipoxvirus recombinant vectors, in order to try to improve the expression of the antigens which coding sequences are in the avipoxvirus vectors.

3.3 In the present application is disclosed that the introduction of a host range gene in a avipoxvirus results in an increase in avipoxvirus titer, which is stated to be a surprising effect.

The IPEA considers that said effect is not surprising. The increase in antigen production would be expected to result in an increase in avipoxvirus titer since increased mRNA stability and protein production (associated in D1 and D2 to the use of E3L) would indeed result in more viral RNA and viral proteins being produced, thus resulting in an higher virus titer.

3.4 Furthermore, even if said effect would have been surprising, it is considered to be a bonus effect. As discussed in sections 3 to 3.2 above, the skilled person would have been motivated to introduce a host range gene in avipoxvirus in order to enhance protein production. The increased virus titer is an additional effect which would be intrinsic to said constructs.

4. For the assessment of the present claims 13 and 14 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The EPO does not recognize as industrially applicable methods of treatment of the human body by surgery or therapy and diagnostic methods practised on the human or animal body. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.